REMARKS

At the outset, the undersigned attorney submits he is submitting this Reply in a representative capacity under 37 CFR §1.34. The registration number, name, and signature of the undersigned attorney is provided at the end of this correspondence. This reply accompanies a Request for Continued Examination under 37 CFR §1.114.

Claims 135-139, 142-146, 148-153, and 155-157 remain in prosecution. Claims 1-134 were cancelled previously, and claims 140, 141, 147, and 154 are herein cancelled without prejudice. Claims 135, 148-153, 155, and 157 are herein amended.

Rejections under 35 USC §112, first paragraph

Claims 135-140, 142-146, 148-153, and 156 were rejected under 35 USC §112, first paragraph, as allegedly failing to comply with the written description requirement.

To address the rejection, Applicants herein amend claim 135 to recite with greater specificity the various components and steps in the claimed method. In particular, claim 135 now recites:

135. A method of predicting the receptor-modulating activity of a test compound when bound to a receptor, comprising the steps of:

(1) (a) providing an estrogen receptor;

(b) contacting said estrogen receptor with a plurality of reference compounds, said reference compounds known to modulate the biological activity of said estrogen receptor, and wherein the binding of each reference compound to said estrogen receptor forms a reference conformation ,said plurality of reference compounds selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182, 780, 16α-OH estrone, and progesterone;

(c) providing a panel comprising a plurality of members representing a plurality of classes selected from the group consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/ ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII, wherein said members of said panel possess differential ability to bind to said reference conformation;

(d) contacting said reference conformation with said panel;

(e) measuring the effect of said reference compound on the binding of said panel members to said receptor, said measuring step forming a fingerprint for each member of said plurality of reference compounds;

(2) (a) providing a test compound;

(b) contacting said estrogen receptor with said test compound, wherein the binding of said test compound to said estrogen receptor forms a test conformation;

(c) contacting said test conformation with said panel;

(d) measuring the effect of said test compound on the binding of said panel member; and

(3) comparing the effect of said test compound on the binding of said panel member to said fingerprints to predict the

receptor-modulating activity of said test compound when bound to said estrogen receptor.

Specifically, claim 135 is amended to recite that an estrogen receptor is employed; that the reference compounds are selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182,780, 16α-OH estrone, and progesterone; and that the recited plurality of members represent a plurality of classes selected from the group consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/ ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII. Support for these claim amendments can be found in original claims 140, 141, 147, and 154, which are herein cancelled. Applicants now submit that these rejections are overcome.

Rejections under 35 USC §112, second paragraph

Claims 135-157 were rejected as being allegedly indefinite for failing to particularly point out and distinctly claim the invention. Applicants respectfully traverse the rejection.

Claim 136 was rejected because the term "panel-based descriptor" was unclear. Applicants submit that "panel-based descriptor" is described in the specification at page 45, first full paragraph, as well as at page 46, line 30 and continuing to page 47, line 8. In particular, the specification discloses

that a descriptor is a numerically expressed characteristic of a compound that distinguishes it from other compounds. Applicants now submit that this rejection is overcome.

Claim 148 was rejected because "Xaa" was unclear. In response, Applicants herein amend claim 148 to positively recite that Xaa refers to any amino acid. Support for this amendment may be found throughout the specification, and particularly at page 132, lines 1-2 where the composition of the LXXLL sequence is disclosed. Applicants now submit that this rejection is overcome.

Double Patenting Rejections

Applicants respectfully thank the Examiner for withdrawing the §101 double patenting rejection over US Patent No. 6,617,114, and the provisional double patenting rejections over US Patent Application Serial Nos. 09/860,688 and 10/332,708.

Claims 135-157 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, and 6 of US Patent No. 6,617,114 and claims 27-29, 32, 35, and 37 of copending US Patent Application Ser. No. 10/346,162. Applicants will submit a suitable Terminal Disclaimer upon indication of allowable subject matter in the present application.

Rejections under 35 USC §103

Claims 135-139, 142-146, and 156 were rejected as being allegedly unpatentable over US Patent No. 5,587,293 to Kauvar et al. Applicants respectfully traverse the rejection.

Kauvar et al. discloses a method to determine reactivity of a candidate compound with a target receptor. The method uses a plurality of different target "reference" receptors to which the reactivity or binding of a number of known compounds is determined to produce a table showing the reactivity of the known compounds against each of the receptors. In Kauvar et al., an unknown compound is tested against the reference receptors to allow a predicted activity against a target receptor had the target receptor itself been used.

To address the rejection, Applicants herein amend claim 135 to recite with greater specificity the various components and steps in the claimed method. Specifically, claim 135 is amended to recite that an estrogen receptor is employed; that the reference compounds are selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182,780, 16α-OH estrone, and progesterone; and that the recited plurality of members represent a plurality of classes selected from the group

consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/ ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII. Support for these claim amendments can be found in original claims 140, 141, 147, and 154, which are herein cancelled.

Applicants submit that Kauvar does not disclose or suggest a method of predicting the receptor-modulating activity of a test compound using the specific combination of (1) an estrogen receptor; (2) a plurality of reference compounds selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182, 780, 16α-OH estrone, and progesterone; and (3) a panel comprising a plurality of members representing a plurality of classes selected from the group consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/ ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII. Accordingly, Applicants now submit that this rejection is overcome.

Claim 140-141, 147-155, and 157 were rejected as being unpatentable over US Patent No. 5,587,293 to Kauvar et al., in view of U.S Patent No. 5,723,291 to Kushner et al. or U.S. Patent No. 5,445,941 to Yang et al. Applicants respectfully traverse the rejection.

Kushner et al. discloses novel assay methods for identifying compounds that may have both estrogen agonist and

antagonist properties. In particular, Kushner et al. disclose assays that use cells comprising promotors having an AP1 site linked to a reporter gene, and compounds capable of inducing or blocking expression of the reporter gene can therefore be identified. Yang et al. discloses methods for screening anti-osteoporosis agents using nucleic acids consisting essentially of the nucleotide sequence of a mammalian promoter comprising a raloxifene responsive element.

In contrast, claim 135 of the present invention recites:

135. A method of predicting the receptor-modulating activity of a test compound when bound to a receptor, comprising the steps of:

(1) (a) providing an estrogen receptor;

(b) contacting said estrogen receptor with a plurality of reference compounds, said reference compounds known to modulate the biological activity of said estrogen receptor, and wherein the binding of each reference compound to said estrogen receptor forms a reference conformation ,said plurality of reference compounds selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen, clomifene, premarin, raloxifene, ICI 182, 780, 16α-OH estrone, and progesterone;

(c) providing a panel comprising a plurality of members representing a plurality of classes selected from the group consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/

ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII, wherein said members of said panel possess differential ability to bind to said reference conformation;

(d) contacting said reference conformation with said panel;

(e) measuring the effect of said reference compound on the binding of said panel members to said receptor, said measuring step forming a fingerprint for each member of said plurality of reference compounds;

(2) (a) providing a test compound;

(b) contacting said estrogen receptor with said test compound, wherein the binding of said test compound to said estrogen receptor forms a test conformation;

(c) contacting said test conformation with said panel;

(d) measuring the effect of said test compound on the binding of said panel member; and

(3) comparing the effect of said test compound on the binding of said panel member to said fingerprints to predict the receptor-modulating activity of said test compound when bound to said estrogen receptor.

Applicants submit that none of the references, taken individually or in combination, disclose or suggest the invention as now claimed, and in particular a method of predicting the receptor-modulating activity of a test compound using the specific combination of (1) an estrogen receptor; (2) a plurality of reference compounds selected from the group consisting of estradiol, estriol, nafoxidine, 4-OH tamoxifen,

clomifene, premarin, raloxifene, ICI 182, 780, 16α-OH estrone, and progesterone; and (3) a panel comprising a plurality of members representing a plurality of classes selected from the group consisting of ERα/ ßI, ERα/ ßII, ERα/ ßIII, ERα/ ßIV, ERαI, ERαII, ERαIII, ER ßI, ERßII, and ERßIII. Accordingly, Applicants now submit that this rejection is overcome.

Any fees or credits due with this response may be charged to Deposit Account 23-1665.

If the Examiner has any questions or feels that a discussion with Applicants' representative would expedite prosecution, the Examiner is invited and encouraged to contact Applicants' undersigned representative at the telephone number listed below.

Respectfully submitted,

LISA A. PAIGE ET AL.

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